a5 cont 36. A recombinant organism according to claim 11 wherein the organism is selected from the group consisting of a microorganism, a mammalian cell, and a plant cell.

REMARKS

Claim 4 has been amended to remove the recitation of "SEQ ID NO 6, SEQ ID NO 7, and SEQ ID NO 8, and amino acid sequences which contain addition, insertion, deletion and/or substitution of one or more amino acid residues in said sequence." Support for this amendment is found in original claim 4 and in the specification at, for example, page 4, lines 8-10, and page 17, lines 14-17. *See, In re Gardner*, 177 USPQ 396, 397 (CCPA 1973) and MPEP §§ 608.01 (o) and (l).

Claim 4 has also been amended to recite "a polypeptide with at least 80% identity to SEQ ID NO:5 and having alcohol and aldehyde dehydrogenase (AADH) activity." Support for this amendment is found in the specification at, for example, Table 7 entitled *Homologies of amino acid sequences among AADHs* on page 34, lines 14-19.

Claim 6 has been amended to remove the recitation of "SEQ ID NO 2, SEQ ID NO 3, and SEQ ID NO 4, and sequences which contain addition, insertion, deletion and/or substitution of one or more nucleotides in said sequence." Support for this amendment is found in original claim 6 and in the specification at, for example, page 16, lines 1-7, and page 17 lines 14-17. (*Id.*).

Claim 6 has also been amended to recite "and DNA sequences which encode a polypeptide with at least 80% identity to SEQ ID NO:5." Support for this amendment is found in the specification at, for example, Table 7 on page 34, lines 14-19.

Claim 7 has been amended to remove the recitation of "SEQ ID NO 2, SEQ ID NO 3, and SEQ ID NO 4, and sequences which contain addition, insertion, deletion and/or substitution of one or more nucleotides in said sequence." Support for this amendment is found in original claim 7 and in the specification at, for example, page 10, line 18 to page 11 line 10 and page 12, lines 21-25. (*Id.*).

Claim 7 has also been amended to recite "and DNA sequences which encode a polypeptide with at least 80% identity to SEQ ID NO:5." Support for this amendment is found in the specification at, for example, Table 7 on page 34, lines 14-19.

Claim 8 has been amended to recite pSSA102R. Support for this amendment is found in original claim 8 and in the specification at, for example, page 35, lines 8-15. (*Id.*).

Claims 10 and 11 have been amended to replace "including" with --comprising-- for purposes of clarity only.

Claim 16 has been amended to remove the recitation of "SEQ ID NO 6, SEQ ID NO 7, SEQ ID NO 8, and amino acid sequences which contain addition, insertion, deletion and/or substitution of one or more amino acid residues in said

sequence." Support for this amendment is found in original claim 16 and in the specification at, for example, page 4, lines 8-12, and page 5, lines 1-14 as well as, page 17, line 14 to page 18, line 20. (*Id.*).

Claim 16 has also been amended to recite a polypeptide "containing an amino acid sequence with at least 80% identity to the polypeptide sequence of SEQ ID NO:5." Support for this amendment is found in the specification at, for example, Table 7 on page 34, lines 14-19.

Claim 29 has been added. Support for this amendment is found in the specification at, for example, page 17, lines 14-17, Table 7 on page 34, lines 14-19, and in the Sequence Listing.

Claim 30 has been added. Support for this amendment is found in the specification at, for example, page 14, lines 8-13 and page 60, lines 12-15 and in the Sequence Listing.

Claim 31 has been added. Support for this amendment is found in the specification at, for example, page 14, lines 8-13 and page 60, lines 11-12 and in the Sequence Listing and Figure 4.

Claim 32 has been added. Support for this amendment is found in the specification at, for example, page 14, lines 8-13 and page 60, lines 5-14 and in the Sequence Listing and Figure 4.

Claim 33 has been added. Support for this amendment is found in original claim 8 and in the specification at, for example, page 5, lines 1-4 and page 35, lines 8-15. (*Id.*).

Claim 34 has been added. Support for this amendment is found in original claim 8 and in the specification at, for example, page 5, lines 1-4. (*Id.*).

Claims 35 and 36 have been added to depend from claims 10 and 11, respectively, and further define the recombinant microorganism. Support for these claims is found in the specification at, for example, page 10, lines 18-26.

It is submitted that no new matter has been introduced by the foregoing amendments. Approval and entry of the amendments is respectfully solicited.

Written Description Rejection

Claims 4-7 and 10-16 were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter that was not described in the specification in such a way to convey that the inventors, at the time the application was filed, had possession of the claimed invention. (Paper No. 13 at 4). In making the rejection, the Examiner contended that "[n]o information, beyond the characterization of SEQ ID NO:5 has been provided" and that "[t]he disclosure does not set forth DNA molecules encoding recombinant polypeptides having a sequence comprising SEQ ID NO:5 and any number of amino acid sequences which contain addition, insertion, deletion, and/or substitution of one or more amino acids residues in SEQ ID NO:5." (*Id.*).

With a view towards furthering prosecution, claims 4, 6, 7, and 16 have been amended to remove the language objected to by the Examiner. In view of these amendments, the rejection is rendered moot and should be withdrawn.

Enablement Rejections

Claims 4-7 and 10-16 were rejected under 35 U.S.C. §112, first paragraph. (Paper No. 13 at 5). In making the rejection, the Examiner acknowledged that the specification was enabling for the DNA molecules of SEQ ID NO:1 and SEQ ID NO:5, as well as for chimeric genes thereof, but that the specification "does not reasonably provide enablement for . . . any number of sequences produced by addition, insertion, deletion and/or substitution of one or more nucleotides in SEQ ID NO:1." (*Id.*).

With a view towards furthering prosecution, claims 4, 6, 7, and 16 have been amended to remove the language objected to by the Examiner. In view of these amendments, the rejection is rendered moot and should be withdrawn.

Claim 8 was rejected under 35 U.S.C. §112, first paragraph. (Paper No. 13 at 6). In making the rejection, the Examiner asserts that the recombinant expression vector pSSA102R is not enabled by the specification. (*Id.*). The Examiner further asserts that because "the pSSA102R vector is essential to the claimed invention, it must be ***obtainable by a repeatable method*** set forth in the specification or otherwise readily available to the public." (*Id.*). The Examiner also asserts that the claimed vector sequences are not fully disclosed, nor have all sequences required for the vector construction been shown to be publicly known and freely available. (*Id.*). Next, the

Examiner asserts that the specification does not disclose ***a repeatable process*** to obtain the vector and "***it is not apparent***" if the DNA sequences are readily available to the public. (*Id.*). Thus, the Examiner concludes that a deposit of pSSA102R is required. (*Id.*).

For the reasons set forth below, the rejection is respectfully traversed.

As is fundamental, an application must describe the claimed invention in sufficient detail to enable any person skilled in the relevant art to make and use the full scope of the claimed invention without undue experimentation. *See* 35 USC §112, first paragraph ("The specification shall contain a written description of the invention, and of the manner and process of making and using it, ... to enable any person skilled in the art ... to make and use the same ....").

Whether a claim is sufficiently enabled by a disclosure in a specification is a question of law based on underlying factual inquiries, and is determined as of the date that the patent application was first filed, *i.e.*, its effective filing date. *In re Hogan*, 194 USPQ 527, 535 (CCPA 1977). Enablement may be satisfied by combining what is disclosed in a specification with what is known in the prior art. *In re Strahilevitz*, 212 USPQ 561, 564 (CCPA 1982).

Although not explicitly set forth in the statute, enablement may be found where some experimentation (even a considerable amount) is required, so long as the experimentation is not "undue." The Board of Patent Appeals and Interferences addressed this issue in the context of deciding whether a genetically engineered organism must be deposited if the original strain from which the genetically engineered

strain is derived is publicly available. *Ex parte Forman*, 230 USPQ 546 (B.P.A.I. 1986). The Federal Circuit adopted the *Forman* analysis in another enablement case stating that:

> ***The factors to be considered have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims.***

In re Wands. 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

It is well settled that the Examiner bears the burden to demonstrate that a specification is not sufficiently enabling. *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971). To carry her burden, the Examiner must identify and clearly articulate the ***factual bases and supporting evidence*** that allegedly establish that undue experimentation would be required to carry out the claimed invention. *Id.* at 370.

Here, the Examiner has identified what "is not disclosed" in the specification; but has failed to consider the full disclosure of the application in conjunction with the level of skill in the art. Moreover, the Examiner uses "repeatable process" and "not apparent" standards in making the rejection. As noted above, however, the correct standard is whether the disclosure enables one skilled in the art to make the claimed invention without undue experimentation. Focusing on whether something is repeatable or not apparent is inconsistent with the settled law that the

analysis should be on whether undue experimentation is required to make the claimed invention. Thus, the rejection is insufficient as a matter of law. For this reason alone, the rejection should be withdrawn.

Enablement is an intensely factual determination, which is why an Examiner is required to clearly articulate her reasons for rejecting a claim under this provision, and to support her reasoning with evidence. (*See* MPEP §2164.04 at 2100-178 to 2100-179). This the rejection has not done. For the Examiner's convenience, we identify below, consistent with the Federal Circuit's *In re Wands* decision, facts which were not considered in the rejection and which support the conclusion that it would ***not*** require undue experimentation to make or use the pSSA102R vector recited in claim 8.

First, claim 8, as amended recites a single, specific vector, pSSA102R. Second, although certain areas of biotechnology may be characterized as "unpredictable," here the claim is directed to a vector. The technology required to make vectors is well settled, and there is nothing that is unduly burdensome about such a process once the vector is identified, the insert sites in the vector are identified, and the nucleotide sequence to be inserted into the vector is identified.

Third, the level of skill in this art is very high. A person skilled in this art likely has a graduate degree in molecular biology and several years of experience.

Fourth, vector construction is not new to biotechnology. This is a fundamental technology that is used everyday in the lab. Vector construction is routine when the vector itself is identified, the insert is identified, and the vector splice sites are

identified. Fifth, the claimed invention is a vector containing a novel polynucleotide, which polynucleotide is fully described in the specification.

Six, the application contains 15 examples and ample instructions/directions to make the claimed vector. For example, Example 1 describes the cloning of the polynucleotide insert used in pSSA102R. Example 2 describes the sequencing of the nucleotides encoding Enzyme A (as well as A', A'', and B). And, Example 3 specifically discloses how pSSA102R is derived: "The 2.7 kb *Eco*RV fragment which includes ORF of Enzyme A gene with about 500 bp of non-coding regions at both the ends was excised from 3.4 kb *Nru*I fragment, which was isolated from p24D4 in M13 mp18, and was ligated to *Hind*III site of pUC18 with *Hind*III linker (CAAGCTTG). The resulting plasmid was designated pSSA202. Enzyme A gene cassette (2.7 kb HindIII fragment) was then inserted at HindIII site of pVK102 to produce pSSA102R." (page 35, lines 10-15). And, pVK102 is a cosmid vector that is identified in the specification by its ATCC number (ATCC37158). (page 27, line 25). Figure 2 also provides a graphical representation of the vector construction. We also note that Fig. 7 provides a restriction map of Enzyme A.

In view of the foregoing, one skilled in this art could readily make the claimed vector in view of the disclosure of the vector itself, the vector insert, the restriction sites, and the restriction map of Enzyme A encoded by the polynucleotide insert. Thus, a deposit of pSSA102R is not required to fulfill the enablement provision of §112, first paragraph.

In sum, the rejection is insufficient as a matter of fact and law, and should be withdrawn for the reasons set forth above.

Anticipation Rejection

Claims 4-7 and 10-16 were rejected under 35 USC §102(b) as anticipated by Tamaki *et al.*, EP 448969 ("Tamaki"). (Paper No. 13 at 7).

Tamaki discloses a gene for a membrane-bound alcohol dehydrogenase obtained from *Acetobacter altocetigenes*.

In making the rejection, the Examiner contended that "the sequence of the gene [from Tamaki] has 2217 nucleotides and ***55% best local similarity*** to SEQ ID NO:1 of the instant application. Thus the gene disclosed in the [Tamaki] patent anticipates the DNA of SEQ ID NO:1 of the instant application with one or more nucleotides added, deleted and/or substituted." (Paper No. 13 at 7).

With a view towards furthering prosecution, claims 4, 6, 7, and 16 have been amended to remove the recitation of "addition, insertion, deletion, and/or substitution of one or more nucleotides or amino acid residues." And, claims 4, 6, 7, and 16 have also been amended to recite "DNA sequences which encode a polypeptide with ***at least 80% identity*** to SEQ ID NO:5."

Thus, the rejection does not and cannot identify where in Tamaki there is disclosed SEQ ID NO:5 or DNA sequences which encode a polypeptide with ***at least 80% identity*** to SEQ ID NO:5 as recited by amended claims 4, 6, 7, and 16. Thus, the rejection has been rendered moot, and should be withdrawn.

For the reasons set forth above, entry of the amendments, withdrawal of the rejections, and allowance of the claims is respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to Commissioner for Patents, Washington, DC 20231 on February 28, 2002.

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Respectfully submitted,

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In re Application of : Akira ASAKURA *et al.*
U.S. Serial No.: 09/470,667
For: NOVEL ALCOHOL/ALDEHYDE DEHYDROGENASES

Exhibit 1

"Marked Up" Amendments to Claims Pursuant to Rule 1.121(c)

4. (Amended) A DNA molecule encoding a recombinant polypeptide comprising [containing an amino acid sequence selected from the group consisting of] SEQ ID NO:5 or a polypeptide with at least 80% identity to SEQ ID NO:5, and having alcohol and aldehyde dehydrogenase (AADH) activity [NO 5, SEQ ID NO 6, SEQ ID NO 7, SEQ ID NO 8, and amino acid sequences which contain addition, insertion, deletion and/or substitution of one or more amino acid residues in said sequence].

6. (Amended) A recombinant expression vector comprising [at least one DNA molecule containing] a DNA sequence selected from the group consisting of SEQ ID NO:1 and DNA sequences which encode a polypeptide with at least 80% identity to SEQ ID NO:5 and having [NO 1, SEQ ID NO 2, SEQ ID NO 3, SEQ ID NO 4, and sequences which contain addition, insertion, deletion and/or substitution of one or more nucleotides in said sequence, said DNA molecule encoding a recombinant polypeptide having an] alcohol and aldehyde dehydrogenase activity.

7. (Amended) A recombinant expression vector comprising [at least one DNA molecule containing] a DNA sequence selected from the group consisting of SEQ ID NO:1 and DNA sequences which encode a polypeptide with at least 80% identity to

SEQ ID NO:5, [NO 1, SEQ ID NO 2, SEQ ID NO 3, SEQ ID NO 4, and sequences which contain addition, insertion, deletion and/or substitution of one or more nucleotides in said sequence, said DNA molecule encoding a recombinant polypeptide having an alcohol and aldehyde dehydrogenase activity,] wherein the DNA sequence [said at least one DNA molecule] is functionally linked to one or more genetic control sequences and is capable of expression of an enzyme including at least one recombinant polypeptide having alcohol and aldehyde dehydrogenase activity.

8. (Amended) A recombinant expression vector of claim 7 which is [selected from the group consisting of] pSSA102R [pSSA'101R, pSSA"102, pSSB103R, pSSA^{P}-B, pSSA/B101R, pSSA/B102R, pSSA/B103R, pSSB/A101R, pSSB/A102R, pSSB/A103R, pSSsA2, pSSsA21, PSSsA22 and PSSsB].

10. (Amended) A recombinant organism comprising [including] the recombinant expression vector of claim 6.

11. (Amended) A recombinant organism comprising the [including the at least] DNA molecule of claim 4.

16. (Amended) A process for producing a recombinant enzyme having an alcohol and aldehyde dehydrogenase activity comprising:

a) culturing a recombinant organism comprising **[**including**]** an expression vector comprising a **[**including at least one**]** DNA molecule encoding a recombinant polypeptide containing an amino acid sequence with at least 80% identity to the polypeptide sequence **[**selected from the group consisting**]** of SEQ ID NO:5 **[**NO 5, SEQ ID NO 6, SEQ ID NO 7, SEQ ID NO 8, and amino acid sequences which contain addition, insertion, deletion and/or substitution of one or more amino acid residues in said sequence,**]** in an appropriate culture medium; and

b) recovering the **[**said**]** recombinant enzyme.